

# SEQUENCE LISTING

<110> Adolf, Guenther  
 Baum, Anke  
 Heider, Karl-Heinz

<120> Compositions and Methods for Treating Cancer using  
 Cytotoxic CD44 Antibody Immunoconjugates and  
 Chemotherapeutic Agents

<130> 1/1383

<140> To be assigned  
 <141> 2003-08-21

<150> EP 02 018 686.2  
 <151> August 21, 2002

<150> US 60/405,956  
 <151> August 26, 2002

<160> 9

<170> PatentIn Ver. 2.1

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 <211> 42  
 <212> PRT  
 <213> Homo sapiens

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 Glu Asp Ser His Ser Thr Thr Gly Thr Ala  
 35 40

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 <212> PRT  
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<220>  
<223> Humanised Murine Antibody BIWA 4 Light Chain

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Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly  
1 5 10 15  
Glu Arg Ala Thr Leu Ser Cys Ser Ala Ser Ser Ser Ile Asn Tyr Ile  
20 25 30  
Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr  
35 40 45  
Leu Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser  
50 55 60  
Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu  
65 70 75 80  
Asp Phe Ala Val Tyr Tyr Cys Leu Gln Trp Ser Ser Asn Pro Leu Thr  
85 90 95  
Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro  
100 105 110  
Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr  
115 120 125  
Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys  
130 135 140  
Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu  
145 150 155 160  
Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser  
165 170 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala  
180 185 190

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe  
195 200 205

Asn Arg Gly Glu Cys  
210

<210> 5  
<211> 702  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Humanised Murine Antibody BIWA 4 Light Chain

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gaaattgttc tcaccagtc tccagcaacc ctgtctctgt ctccagggga gagggccacc 120  
ctgtcctgca gtgccagctc aagtataaat tacatatact ggtaccagca gaagccagga 180  
caggctccta gactcttgat ttatctcaca tccaacctgg cttctggagt ccctgcgcgc 240  
ttcagtggca gtgggtcttg aaccgaactc actctcacia tcagcagcct ggagcctgaa 300  
gattttgccg tttattactg cctgcagtgg agtagtaacc cgctcacatt cgggtggtggg 360  
accaaggtgg agattaaacg tacggtggct gcaccatctg tcttcattct cccgccatct 420  
gatgagcagt tgaaatctgg aactgcctct gttgtgtgcc tgctgaataa cttctatccc 480  
agagaggcca aagtacagtg gaaggtggat aacgccctcc aatcgggtaa ctcccaggag 540  
agtgtcacag agcaggacag caaggacagc acctacagcc tcagcagcac cctgacgctg 600  
agcaaagcag actacgagaa acacaaagtc tacgcctgcg aagtcaccca tcagggcctg 660  
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<212> PRT  
<213> Artificial Sequence

<220>  
<223> Humanised Murine Antibody BIWA 4 Heavy Chain

<400> 6  
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly  
1 5 10 15  
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr  
20 25 30  
Asp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val  
35 40 45  
Ser Thr Ile Ser Ser Gly Gly Ser Tyr Thr Tyr Tyr Leu Asp Ser Ile

| 50         |            |            |            |            | 55         |            |            |            |            | 60         |            |            |            |            |            |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| Lys<br>65  | Gly        | Arg        | Phe        | Thr        | Ile<br>70  | Ser        | Arg        | Asp        | Asn        | Ala<br>75  | Lys        | Asn        | Ser        | Leu        | Tyr<br>80  |
| Leu        | Gln        | Met        | Asn        | Ser<br>85  | Leu        | Arg        | Ala        | Glu        | Asp<br>90  | Thr        | Ala        | Val        | Tyr        | Tyr<br>95  | Cys        |
| Ala        | Arg        | Gln        | Gly<br>100 | Leu        | Asp        | Tyr        | Trp        | Gly<br>105 | Arg        | Gly        | Thr        | Leu        | Val<br>110 | Thr        | Val        |
| Ser        | Ser        | Ala<br>115 | Ser        | Thr        | Lys        | Gly        | Pro<br>120 | Ser        | Val        | Phe        | Pro        | Leu<br>125 | Ala        | Pro        | Ser        |
| Ser        | Lys<br>130 | Ser        | Thr        | Ser        | Gly        | Gly<br>135 | Thr        | Ala        | Ala        | Leu        | Gly        | Cys        | Leu        | Val        | Lys        |
| Asp<br>145 | Tyr        | Phe        | Pro        | Glu        | Pro<br>150 | Val        | Thr        | Val        | Ser        | Trp        | Asn        | Ser        | Gly        | Ala        | Leu<br>160 |
| Thr        | Ser        | Gly        | Val        | His<br>165 | Thr        | Phe        | Pro        | Ala        | Val<br>170 | Leu        | Gln        | Ser        | Ser        | Gly        | Leu<br>175 |
| Tyr        | Ser        | Leu        | Ser<br>180 | Ser        | Val        | Val        | Thr        | Val<br>185 | Pro        | Ser        | Ser        | Ser        | Leu<br>190 | Gly        | Thr        |
| Gln        | Thr<br>195 | Tyr        | Ile        | Cys        | Asn        | Val        | Asn<br>200 | His        | Lys        | Pro        | Ser        | Asn<br>205 | Thr        | Lys        | Val        |
| Asp<br>210 | Lys        | Lys        | Val        | Glu        | Pro        | Lys<br>215 | Ser        | Cys        | Asp        | Lys        | Thr<br>220 | His        | Thr        | Cys        | Pro        |
| Pro<br>225 | Cys        | Pro        | Ala        | Pro        | Glu<br>230 | Leu        | Leu        | Gly        | Gly        | Pro<br>235 | Ser        | Val        | Phe        | Leu        | Phe<br>240 |
| Pro        | Pro        | Lys        | Pro        | Lys<br>245 | Asp        | Thr        | Leu        | Met        | Ile<br>250 | Ser        | Arg        | Thr        | Pro        | Glu        | Val<br>255 |
| Thr        | Cys        | Val        | Val<br>260 | Val        | Asp        | Val        | Ser        | His<br>265 | Glu        | Asp        | Pro        | Glu        | Val<br>270 | Lys        | Phe        |
| Asn        | Trp        | Tyr<br>275 | Val        | Asp        | Gly        | Val        | Glu<br>280 | Val        | His        | Asn        | Ala        | Lys<br>285 | Thr        | Lys        | Pro        |
| Arg<br>290 | Glu        | Glu        | Gln        | Tyr        | Asn        | Ser<br>295 | Thr        | Tyr        | Arg        | Val        | Val        | Ser        | Val        | Leu        | Thr        |
| Val<br>305 | Leu        | His        | Gln        | Asp        | Trp<br>310 | Leu        | Asn        | Gly        | Lys        | Glu<br>315 | Tyr        | Lys        | Cys        | Lys        | Val<br>320 |
| Ser        | Asn        | Lys        | Ala        | Leu<br>325 | Pro        | Ala        | Pro        | Ile        | Glu<br>330 | Lys        | Thr        | Ile        | Ser        | Lys<br>335 | Ala        |

Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg  
                   340                  345                  350  
 Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly  
                   355                  360                  365  
 Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro  
           370                  375                  380  
 Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser  
 385                  390                  395                  400  
 Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln  
                   405                  410                  415  
 Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His  
                   420                  425                  430  
 Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys  
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<210> 7  
 <211> 1392  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Humanised Antibody BIWA 4 Heavy Chain

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 tgtgcagcct ctggattcac tttcagtagc tatgacatgt cttgggttcg ccaggctccg 180  
 gggaagggggc tggagtgggt ctcaaccatt agtagtggtg gtagttacac ctactatcta 240  
 gacagtataa agggccgatt caccatctcc agagacaatg ccaagaactc cctgtacctg 300  
 caaatgaaca gtctgagggc tgaggacacg gccgtgtatt actgtgcaag acagggggtg 360  
 gactactggg gtcgaggaac cttagtcacc gtctcctcag ctagcaccaa gggcccatcg 420  
 gtcttcccc tggcaccctc ctccaagagc acctctgggg gcacagcggc cctgggctgc 480  
 ctgggtcaagg actacttccc cgaaccgggtg acgggtgtcgt ggaactcagg cgccctgacc 540  
 agcggcgtgc acaccttccc ggctgtccta cagtcctcag gactctactc cctcagcagc 600

gtggtgaccg tgcctccag cagcttgggc acccagacct acatctgcaa cgtgaatcac 660  
 aagcccagca acaccaaggt ggacaagaaa gttgagccca aatcttgtga caaaactcac 720  
 acatgcccac cgtgcccagc acctgaactc ctgggggggac cgtcagtctt cctcttcccc 780  
 ccaaaaccca aggacaccct catgatctcc cggacccttg aggtcacatg cgtggtggtg 840  
 gacgtgagcc acgaagaccc tgagggtcaag ttcaactggg acgtggacgg cgtggaggtg 900  
 cataatgcca agacaaagcc gcgggaggag cagtacaaca gcacgtaccg tgtgggtcagc 960  
 gtcctcaccg tcctgcacca ggactggctg aatggcaagg agtacaagtg caaggtctcc 1020  
 aacaaagccc tcccagcccc catcgagaaa accatctcca aagccaaagg gcagccccga 1080  
 gaaccacagg tgtacaccct gcccccatcc cgggatgagc tgaccaagaa ccagggtcagc 1140  
 ctgacctgcc tgggtcaaagg cttctatccc agcgacatcg ccgtggagtg ggagagcaat 1200  
 gggcagccgg agaacaacta caagaccagc cctcccgtgc tggactccga cggctccttc 1260  
 ttctctaca gcaagctcac cgtggacaag agcaggtggc agcaggggaa cgtcttctca 1320  
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<210> 8

<211> 213

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanised Antibody BIWA 8 Light Chain

<400> 8

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| Glu | Ile | Val | Leu | Thr | Gln | Ser | Pro | Ala | Thr | Leu | Ser | Leu | Ser | Pro | Gly |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Glu | Arg | Ala | Thr | Leu | Ser | Cys | Ser | Ala | Ser | Ser | Ser | Ile | Asn | Tyr | Ile |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Tyr | Trp | Leu | Gln | Gln | Lys | Pro | Gly | Gln | Ala | Pro | Arg | Ile | Leu | Ile | Tyr |
|     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Leu | Thr | Ser | Asn | Leu | Ala | Ser | Gly | Val | Pro | Ala | Arg | Phe | Ser | Gly | Ser |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Gly | Ser | Gly | Thr | Asp | Phe | Thr | Leu | Thr | Ile | Ser | Ser | Leu | Glu | Pro | Glu |
| 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     | 80  |     |

Asp Phe Ala Val Tyr Tyr Cys Leu Gln Trp Ser Ser Asn Pro Leu Thr  
                     85                    90                    95  
 Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro  
                     100                    105                    110  
 Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr  
                     115                    120                    125  
 Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys  
                     130                    135                    140  
 Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu  
 145                    150                    155                    160  
 Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser  
                     165                    170                    175  
 Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala  
                     180                    185                    190  
 Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe  
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 Asn Arg Gly Glu Cys  
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<210> 9

<211> 702

<212> DNA

<213> Artificial Sequence

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<220>

<223> Humanised Antibody BIWA 8 Light Chain

<400> 9

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 ctgtcctgca gtgccagctc aagtataaat tacatatact ggctccagca gaagccagga 180  
 caggctccta gaatcttgat ttatctcaca tccaacctgg cttctggagt ccctgcgcgc 240  
 ttcagtggca gtgggtctgg aaccgacttc actctcacia tcagcagcct ggagcctgaa 300  
 gattttgccg tttattactg cctgcagtgg agtagtaacc cgctcacatt cggtgggtggg 360  
 accaaggtgg agattaaacg tacggtggct gcaccatctg tcttcatctt cccgccatct 420

gatgagcagt tgaaatctgg aactgcctct gttgtgtgcc tgctgaataa cttctatccc 480  
agagaggcca aagtacagtg gaaggtggat aacgccctcc aatcgggtaa ctcccaggag 540  
agtgtcacag agcaggacag caaggacagc acctacagcc tcagcagcac cctgacgctg 600  
agcaaagcag actacgagaa acacaaagtc tacgcctgcg aagtcaccca tcagggcctg 660  
agctcgcccg tcacaaagag cttcaacagg ggagagtgtt ga 702